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Dear Sir:

Transmitted herewith for filing is the patent application of:

INVENTORS: Richard FOTLAND, John BOWERS, and William JAMESON

FOR: METHOD AND APPARATUS FOR PRODUCING UNIFORM SMALL PORTIONS  
OF FINE POWDERS AND ARTICLES THEREOF

Enclosed are the following:

- Letter: Submission of Incomplete Application
- Specification 19 pages; Claims 10 pages; Abstract 1 page
- 4 sheet(s) of drawings

The filing fee has been calculated as shown below:

		SMALL ENTITY	LARGE ENTITY
BASIC FEE:		\$380.00	\$760.00
TOTAL CLAIMS:	73 - 20 =	x 11 = \$	x 18 = \$954.00
INDEPENDENT CLAIMS:	6 - 3 =	x 41 = \$	x 78 = \$234.00
MULT. DEPEND. CLAIMS:		+ 135 = \$	+ 270 = \$
TOTAL:		\$	\$1948.00

- A check in the amount of \$1,948.00 is enclosed to cover the fees.

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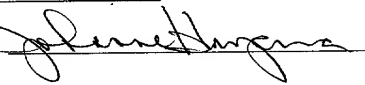
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1 METHOD AND APPARATUS FOR PRODUCING UNIFORM SMALL PORTIONS  
2 OF FINE POWDERS AND ARTICLES THEREOF

3 Background of the Invention

4 This invention is directed towards the deposition of small (usually fractional  
5 gram) masses on a generally electrically non-conductive substrate. One of the most  
6 common methods for accomplishing the goal is practiced by manufacturers of  
7 photocopiers and electrophotographic electronic printers. This involves causing  
8 charged toner particles to migrate with an electric field to a charged area on a  
9 photoreceptor, so-called electrostatic deposition. While electrostatic deposition has  
10 been proposed for packaging powdered drugs (see US Patent Nos. 5,669,973 and  
11 5,714,007 to Pletcher), electrostatic deposition is limited by the amount of mass that can  
12 be deposited in a given area.

13 This limitation is intrinsic to electrostatic deposition technology and is  
14 determined by the combination of the amount of charge that can be placed on the  
15 photoreceptor and the charge to mass ratio of the toner particles. The mass that can be  
16 deposited in an area of a substrate is limited to the charge in the area divided by the  
17 charge to mass ratio of the particles being deposited. The maximum amount of charge  
18 that can be deposited in an area of a substrate is determined by the substrate electrical  
19 properties, the electrical and breakdown properties of the air or gas over it, and by the  
20 properties of mechanism used for charging the substrate. Likewise, the minimum  
21 charge to mass ratio of particles (which determines the maximum mass that can be

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1 deposited) is determined by the charging mechanism. However, as the charge to mass  
2 ratio is decreased, the variation in the charge to mass ratio increases even to the point  
3 where some particles may be oppositely charged relative to the desired charge on the  
4 particles. This variation prevents the reliable deposition of a controlled mass on the  
5 substrate. Furthermore, low charge to mass ratio particles limit the overall speed of  
6 deposition because the force of a particle, which sets the particle velocity, from an  
7 electrostatic field is proportional to the charge carried by the particle. For these reasons,  
8 higher charge to mass ratio particles are generally preferred.

9       Packaged pharmaceutical doses, in the range of 15 to 6000  $\mu\text{g}$  are employed in  
10 dry powder inhalers for pulmonary drug delivery. A mean particle diameter of  
11 between 0.5 and 6.0  $\mu\text{m}$  is necessary to provide effective deposition within the lung. It  
12 is important that the dose be metered to an accuracy of  $\pm 5\%$ . A production volume  
13 of several hundred thousand per hour is required to minimize production costs. High  
14 speed weighing machines are generally limited to dose sizes over about 5,000  $\mu\text{g}$  and  
15 thus require the active pharmaceutical be diluted with an excipient, such as lactose  
16 powder, to increase the total measured mass. This approach is subject to limitations in  
17 mixing uniformity and the aspiration of extraneous matter. Hence, electrostatic  
18 deposition of such pharmaceutical powders is highly desirable.

19       US Patent 3,997,323, issued to Pressman et al, describes an apparatus for  
20 electrostatic printing comprising a corona and electrode ion source, an aerosolized  
21 liquid ink particles that are charged by the ions from the ion source, a multi-layered

1 aperture interposed between the ion source and the aerosolized ink for modulating the  
2 flow of ions (and hence the charge of the ink particles) according to the pattern to be  
3 printed. The charged ink particles are accelerated in the direction of the print receiving  
4 medium. This patent discusses the advantages in the usage of liquid ink particles as  
5 opposed to dry powder particles in the aerosol. However, from this discussion it is  
6 apparent, aside from the disadvantages, that dry powder particles may also be used.  
7 Furthermore, the charge to mass ratios achieved from using an ion source for charging  
8 the powder particles are much higher than those generally achieved using triboelectric  
9 charging (commonly used in photocopies and detailed by Pletcher et al in US Patent  
10 5,714,007), thereby overcoming the speed issue discussed above. Such printers have  
11 been commercially marketed and sold. However, an apparatus for depositing powder  
12 on a dielectric (i.e. a powder carrying package) using the Pressman approach also  
13 suffers from the above described maximum amount of powder that can be deposited on  
14 the dielectric. This is because during the deposition process, charge from both the ions  
15 and the charged particles accumulates on the dielectric, ultimately resulting in an  
16 electric field that prevents any further deposition. In other words, the amount of  
17 material that can be deposited on the dielectric packaging material is limited by the  
18 amount of charge that can be displaced across it which is determined by the capacitance  
19 of the dielectric and the maximum voltage that can be developed across it.

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2 SUMMARY OF THE INVENTION

3 The above disadvantages are overcome in the present invention by providing an  
4 alternating electric field for depositing particles onto a dielectric substrate. More  
5 particularly, the present invention comprises a method and apparatus for depositing  
6 particles from an aerosol onto a dielectric substrate wherein the method comprises and  
7 the apparatus embodies the following steps: charging the aerosol particles, positioning  
8 them in a deposition zone proximate to the dielectric, and applying an alternating field  
9 to the deposition zone by which the aerosol particles are removed from the aerosol and  
10 deposited on the dielectric substrate thus forming a deposit. The alternating field  
11 provides the means to deposit charged particles and/or ions such that the accumulation  
12 of charge on the dielectric substrate does not prevent further deposition of particles  
13 thus enabling electrostatic deposition of a deposit with relatively high mass.

14 In one embodiment of the invention, the particles are alternately charged in  
15 opposite polarities and deposited on the substrate with the alternating electric field,  
16 thus preventing charge accumulation on the dielectric substrate.

17 In a second embodiment, an ion source is provided in the deposition zone to  
18 provide ions of both polarities for charging the particles. The alternating field  
19 determines which polarity of ions is extracted from the ion source. These extracted ions  
20 may be used for charging the particles and/or discharging the deposited particles on  
21 the dielectric substrate.

1 In a third embodiment substantially all of the particles are removed from the  
2 aerosol. In this embodiment, the mass of the deposit is controlled by measuring the  
3 mass flow into the deposition zone and controlling the deposition time to accumulate  
4 the desired mass of deposit.

5 In yet another embodiment, the mass of the deposit is determined by measuring  
6 the mass flow both into the deposition zone and immediately downstream thereof, and  
7 the difference being the amount deposited.

#### 8 BRIEF DESCRIPTION OF THE DRAWINGS

9 The foregoing and other advantages of the present invention will become  
10 apparent from the following description taken together with the accompanying  
11 drawings in which:

12 FIG. 1 depicts a schematic cross section of a deposition apparatus made in  
13 accordance with the present invention;

14 FIG. 2 illustrates voltage differences in the deposition apparatus of FIG. 1;

15 FIG. 3 depicts an article made in accordance with the present invention; and

16 FIGS. 4 to 7 depict schematic views of various preferred embodiments of the  
17 present invention.

#### 18 DETAILED DESCRIPTION

19 The present invention provides a method and apparatus for depositing a  
20 relatively large mass of material upon a dielectric substrate and the resulting deposition  
21 product. The general apparatus for carrying out this deposition is shown in FIG. 1 and

includes a first electrode 5, a dielectric substrate 1 closely proximate to or in contact with a second electrode 3, also herein referred to as a deposition electrode. The volume between the dielectric substrate 1 and the first electrode 5 comprises a deposition zone into which aerosol particles are introduced. This is indicated by the horizontal arrow of FIG. 1. An alternating electric field (the deposition field), indicated by the vertical arrow in FIG. 1 is created within the deposition zone by first electrode 5, second electrode 3 in combination with an alternating voltage source, shown in FIG. 1 as comprising batteries 9 and 11 and switch 7 wherein the polarity of the field generating voltage is determined by the position of switch 7. However, any suitable means for generating an alternating voltage is contemplated to be within the scope of the invention. Charged particles from the aerosol within the deposition zone are electrostatically attracted to the substrate 1 thereby forming a deposit 15 as shown in FIG. 2. The deposit is incrementally formed from groups of particles deposited from each cycle of the alternating field thereby forming a deposit with a relatively larger mass than is possible if a static electric field were to be used. The process of forming the deposit may be terminated by removal of the alternating field. The completed deposit is shown in FIG. 3 as deposited on the dielectric substrate 1.

The aerosol particles may comprise a dry powder or droplets of a liquid. In one particular embodiment of this invention, the particles comprise a pharmaceutical, for example, albuterol. The pharmaceutical deposits made from deposited pharmaceutical particles may, for example, form a dosage used in a dry powder inhaler. In a second

embodiment of this invention, the particles comprise a carrier coated with a biologically active agent. An example of a bioactive agent coated carrier is a gold particle (the carrier) coated by fragments of DNA (the bioactive agent). Such particles are used for gene therapy. The prior examples are intended to exemplify the applications of the invention, and not intended to limit the scope of it.

The aerosol gas may comprise air or any other suitable gas or gas mixture. For some applications where it is desired to control precisely the environment to which the particles are exposed, and/or to control ion emission characteristics (discussed subsequently), pure nitrogen, or nearly pure nitrogen mixed with a small percentage of another gas, e.g. carbon dioxide, is preferred.

Basic components of an aerosol generator include means for continuously metering particles, and means for dispersing the particles to form an aerosol. A number of aerosol generators have been described in the literature and are commercially available. The most common method of dispersing a dry powder to form an aerosol is to feed the powder into a high velocity air stream. Shear forces then break up agglomerated particles. One common powder feed method employs a suction force generated when an air stream is expanded through a venturi to lift particles from a slowly moving substrate. Powder particles are then deagglomerated by the strong shear force encountered as they pass through the venturi. Other methods include fluidized beds containing relatively large balls together with a chain powder feed to the bed, sucking powder from interstices into a metering gear feed, using a metering blade



1 to scrape compacted powder into a high velocity air stream, and feeding compacted  
2 powder into a rotating brush that carries powder into a high velocity air stream. A  
3 Krypton 85 radioactive source may be introduced into the aerosol stream to equilibrate  
4 any residual charge on the powder. Alpha particles from the source provide a bipolar  
5 source of ions that are attracted to charged powder resulting in the formation of a  
6 weakly charged bipolar powder cloud.

7 Non-invasive aerosol concentration (and mass density for aerosols of known  
8 particle size and specific density) may be determined optically by using right angle  
9 scattering, optical absorption, phase-doppler anemometry, or near forward scattering.  
10 A few commercially available instruments permit the simultaneous determination of  
11 both concentration and particle size distribution.

12 Particles may be charged within or outside of the deposition zone. One  
13 contemplated method of charging particles is triboelectric charging. Triboelectric  
14 charging occurs when the particles are made to come in contact with dissimilar  
15 materials and may be used with the particles are from a dry powder. Triboelectric  
16 charging is well known and widely used as a means to charge toner particles in  
17 photocopying and electrophotographic electronic printing processes. Generally,  
18 triboelectric charging of particles takes place outside of the deposition zone. A  
19 parameter that characterizes the efficacy of particle charging is the charge-to-mass ratio  
20 of particles. This parameter is important as it determines the amount of force that can  
21 be applied to the particle from an electric field, and therefore, the maximum velocity

that particles can achieve during deposition. This, in turn, sets an upper bound to the deposition rate that can be achieved. Charge-to-mass ratios of  $1\mu\text{C}$  to  $50\mu\text{C}$  per gram are achievable when triboelectrically charging  $1\mu\text{m}$  to  $10\mu\text{m}$  diameter particles. Such charge-to-mass ratios are documented for pharmaceuticals by Pletcher et al in U.S. Patent 5,714,007. However, other particle charging methods may achieve charge-to-mass ratios at least ten times greater than is possible with triboelectric charging. Accordingly, it is preferred to use such a method to maximize the velocity of the particles when under influence of the deposition field and the rate at which it is possible to form the deposit.

Generally these methods for applying higher amounts of charge to the particles utilize an ion source to generate an abundance of ions of both or either positive and negative polarities. Some of the negative polarity ions may be electrons. As particles from the aerosol pass in front of the ion source (the charging zone), ions of one polarity are accelerated away from the ion source by an electric field through which the particles travel. Ions that impact the particles attach to the particles. Ions continue to impact the particles until the local electric fields from the ions attached to the particles generate a local electric field of sufficient magnitude to repel the oncoming ions. Figures 5 and 6 illustrate two approaches for generating charging ions as well as the means for providing an accelerating field.

In FIG. 5 ions are generated using corona wire 35. Ions are accelerated through an open mesh screen 39 from an electric field created between open mesh screen 39 and

electrode 25. Housing 37 may be slightly pressurized to prevent the migration of aerosol particles into the corona cavity. Alternatively, the corona source may consist of one or more corona points at the location of corona wire 35. Aerosol enters the charging zone through channel 23. Particles are charged by corona generated ions that pass through the apertures of screen 39. Such a particle charging method is known. A derivative of this method is described by Pressman et al in US Patent 3,977,323. As shown in FIG. 5, electrode 25 is the previously described deposition electrode and open mesh screen is the first electrode of the previously described deposition zone. Likewise, substrate 33 is the previously described dielectric substrate. Thus, in this exemplary configuration, the charging zone and deposition zone are the same and the particles are simultaneously charged and made to deposit. A particle trajectory is shown by path 41.

An alternate particle charging method using an ion source employs a silent electric discharge (SED) charge generator. The construction and operation of this class of device is described by D. Landheer and E.B. Devitts, Photographic Science and Engineering, 27, No. 5, 189-192, September/October, 1993 and also in US Patents 4,379,969, 4,514,781, 4,734,722, 4,626,876 and 4,875,060. In the exemplary implementation illustrated in FIG. 6, a cylindrical glass core 43 supports four glass coated tungsten wires 45 equally spaced about its surface. The assembly is closely wound with a fine wire 47 in the form of a spiral. A typical generator unit, available from Delphax Systems, Canton, MA, consists of a 1cm diameter Pyrex glass rod supporting four glass clad 0.018cm diameter tungsten wires. The assembly is spiral

1 wound with 0.005cm diameter tungsten wire at a pitch of about 40 turns per cm. Only  
2 one glass coated tungsten wire is activated at any time. The other three wires are spares  
3 that may be rotated into the active position if the original active wire becomes  
4 contaminated. In FIG. 6, the active wire is that wire closest to the opening in channel  
5 23. Ions and electrons are generated in the region adjacent the glass coated wire when a  
6 potential of about 2300VACpp at a frequency of about 120 KHz is applied between the  
7 tungsten wire core and the spiral wound tungsten wire. Ions and electrons are  
8 withdrawn from the active region by an electric field created between spiral winding 47  
9 and electrode 25. As in FIG. 5, in the exemplary configuration of FIGS. 6 and 7, the  
10 aerosol particles are simultaneously charged and made to deposit.

11 Other ion sources exist that may be suitable for charging particles. For example,  
12 it is possible to generate ions with X-rays or other ionizing radiation (e.g. from a  
13 radioactive source). When particles are charged with an ion source, any means for  
14 making available ions of both or either positive and negative polarity ions is meant to  
15 be within the scope of the invention.

16 Another means for charging particles particularly applicable to liquid droplets is  
17 described by Kelly in US Patent 4,255,777. In this approach, charged droplets are  
18 formed by an electrostatic atomizing device. Although, the charge-to-mass ratio of such  
19 particles cited by Kelly is not as high as can be achieved when charging particles with  
20 an ion source, it is comparable to that achievable by triboelectric charging and may be

1 both preferable in some applications of the invention and is, in any case, suitable for use  
2 with the present invention.

3 The above cited configurations are not meant to imply any limitations in  
4 configuration. Rather they are meant to serve as examples of possible configurations  
5 contemplated by the invention. Therefore, for example, although particle charging with  
6 ion sources is shown and discussed wherein particles are charged within the deposition  
7 zone, charging of particles with ion sources outside of the deposition zone is also  
8 contemplated. All possible combinations of system configuration made possible by the  
9 present disclosure are contemplated to be within the scope of the invention.

10 The alternating deposition field preferably has a frequency between 1Hz and  
11 10KHz, and most preferably, frequency between 10Hz and 1000Hz, and a magnitude of  
12 between 1KV/cm and 10KV/cm. Other frequencies and magnitudes are possible,  
13 depending upon the system configuration. For example, a higher deposition field  
14 magnitude is possible, generally up to 30KV/cm - the breakdown potential of air and  
15 other gases, but not preferred because it may lead to unexpected sparking. Lower  
16 deposition field magnitudes are not preferred because the velocity of the aerosol  
17 particles in response to the applied field becomes too low. Likewise, an alternating  
18 frequency below 1Hz generally is not preferred for most applications because it is  
19 anticipated that charge buildup on the dielectric substrate may substantially diminish  
20 the magnitude of the deposition field over periods of a second or more. However, there  
21 may be applications where this is not the case. Frequencies of 10KHz and higher

1 generally are not preferred because it is believed that the charged particles will not have  
2 sufficient time to travel through the deposition zone and form the deposition.

3 However, for systems with very small deposition zones, this may not be a factor.

4 The waveform of the deposition field preferably is rectangular. However, it has  
5 been found that triangular and sinusoidal waveforms also are effective in forming  
6 deposits, although generally less so. The waveform has a duty cycle, which is defined  
7 in terms of a preferred field direction. The duty cycle is the percentage of time that the  
8 deposition field is in the preferred field direction. The preferred field direction either  
9 may be positive or negative with respect to the deposition electrode depending upon  
10 the characteristics of a particular system configuration. The duty cycle preferably is  
11 greater than 50% and most preferably 90%. The preferred field direction is that which  
12 maximizes the deposition rate.

13 As previously described, the deposition field is formed between a first electrode  
14 and a second, deposition electrode. The first electrode may or may not be an element of  
15 an ion emitter. In some configurations of the invention use of an ion emitter in the  
16 deposition zone is advantageous in that it helps to discharge the deposited charged  
17 particles thereby preventing the buildup of a field from the deposited charged particles  
18 that repels the further deposition of particles from the aerosol. This is particularly  
19 advantageous when the duty cycle is greater than 50%. Of course, an ion emitter is  
20 required in the deposition zone if the aerosol particles are to be charged within the  
21 deposition zone. However, it is also possible to control the charging of the particles,

1 synchronously with or asynchronously to the alternation of the deposition field such  
2 that the buildup of a particle repelling field from the deposit is minimized.

3 The dielectric substrate is closely proximate to and preferably in contact with the  
4 deposition electrode. By closely proximate is meant that the separation between the  
5 dielectric substrate and the deposition electrode is less than the thickness of the  
6 dielectric substrate. In this way, the charged aerosol particles are directed to land on  
7 the dielectric substrate in an area determined by the contact or closely proximate area of  
8 the deposition electrode. Thus, it is possible to control the location and size of the  
9 deposit.

10 The substrate for the deposit may consist of a dielectric material, such as vinyl  
11 film, or an electrically conducting material such as aluminum foil. As previously  
12 mentioned, as unipolar charged powder is deposited upon the surface of a dielectric, a  
13 large electrical potential is formed which generates an electric field that opposes the  
14 deposition field and deposition is thus self-limiting at rather low masses. If unipolar  
15 charged powder is deposited on the surface of an electrical conductor, then again a  
16 surface potential will be built up but of a lower magnitude than that of a corresponding  
17 insulating substrate. The ratio of the surface voltage of a deposit on an insulating layer  
18 to that of a deposit on the surface of a conducting layer is roughly equal to ratio of the  
19 relative thickness of the dielectric plus the thickness of the deposited powder and the  
20 thickness of the deposited powder layer. The use of alternating deposition to form

1 bipolar layers through the use of ac aerosol charging and ac deposition fields allows  
2 larger masses to be deposited onto the surfaces of conductors.

3 The dielectric substrate may be any material and have any structure suitable to  
4 its other functions. For example, it may be a packaging medium, such as a tablet,  
5 capsule or tublet, or the blister of a plastic or metal foil blister package. The dielectric  
6 substrate may also be a pharmaceutical carrier, for example, a pill or capsule. It may be  
7 any edible material, including chocolate. Alternatively, it may be simply a carrier of the  
8 deposit for carrying it to another location for further processing.

9 We have found with the present invention that it is possible to deposit  
10 substantially all of the aerosol particles that pass through the deposition zone under  
11 conditions where the flow rate of the aerosol is below a maximum. This maximum flow  
12 rate is determined primarily by the magnitude of the deposition field, the charge-to-  
13 mass ratio of the charged particles, and their diameters. The capability to deposit  
14 substantially all of the aerosol particles has been demonstrated for relatively large mass  
15 deposits, much larger than is possible using prior art systems that electrostatically  
16 create deposits. For example, we have deposited several milligrams of lactose powder  
17 into a blister of a blister pack of 6mm diameter. A particular advantage of the present  
18 invention is that there are no limits related to charge-to-mass ratio of the charged  
19 particles nor the amount of charge laid down on a substrate as there are with prior art  
20 systems. The use of an alternating deposition field enables deposition of charge of  
21 either polarity on the combination of substrate and deposit, whether the charge is



1 carried by ions or charged particles. The net deposited charge may be therefore  
2 neutralized if necessary. As such, the limits to the mass of the deposit become  
3 mechanical in nature rather than electrical.

4 The ability to deposit substantially all of the aerosol particles that pass through  
5 the deposition zone provides a new method for controlling the mass of the deposit. In  
6 this method the mass flow of the aerosol particles that pass into and out of the  
7 deposition zone is measured over time by means of sensors 60, 62 located upstream and  
8 downstream of the deposition zone. The results could be recorded for manufacturing  
9 control records and adjustments in flow rate, etc., made as need be to maintain a  
10 desired deposition amount. As previously mentioned there are various known means  
11 for measuring the velocity of an aerosol. In combination, these means enable the  
12 measurement of the mass flow rate. The integration of the mass flow rate over time  
13 gives the total mass. Accordingly, the mass of a deposit may be controlled by  
14 measuring the mass flow of aerosol particles into the deposition zone and upon  
15 reaching a desired deposit mass, removing the presence of the alternating deposition  
16 field. In circumstances wherein a portion of the total aerosol is not deposited as it  
17 passes through the deposition zone, a second measuring instrument may be positioned  
18 immediately after the deposition zone. The difference between the two measurements  
19 represents the total mass deposited from the aerosol as it passes the deposition zone.  
20 The deposit may be controlled by removing the presence of the alternating deposition  
21 field as described previously. Even in cases wherein substantially all of the aerosol

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1 particles are deposited in the deposition area, the existence of a second measuring  
2 instrument provides confirmation of the actual mass deposited, and is of particular  
3 interest in applications where the reliability of the mass deposited is of commercial  
4 interest such as pharmaceutical dosages. The mass of deposits formed by the present  
5 invention is relatively larger than deposits that can be formed with prior art methods  
6 that electrostatically create deposits. On the other hand, they may be much smaller  
7 than masses conveniently created using prior art methods that mechanically weigh or  
8 otherwise mechanically measure or control the mass. As such, the present invention  
9 provides a unique means to address a hitherto unaddressed need.

10 The details of the invention may be further examined by considering FIG. 5.  
11 Here, an aerosol generator 17 forms an air borne particle dispersion that is carried by  
12 enclosed channel 19 to aerosol concentration monitoring station 21. Channel 23 then  
13 carries the aerosol through a region where charging device 31 charges the powder. An  
14 electrostatic field is provided between the charging device 31 and deposition electrode  
15 25. Deposition electrode 25 corresponds to electrode 3 shown in FIG. 1. A dielectric  
16 substrate 27 shown here as a blister pack pocket that collects charged particles deflected  
17 by the electrostatic field. A second concentration monitoring station 29 is employed to  
18 determine how much of the particles have been removed from the aerosol. Under  
19 conditions whereby essentially all of the particles are removed from the air stream, this  
20 second concentration monitor may not be required. The air stream then moves into

1 collector 30. This collector might consist of a filter or an electrostatic precipitator or  
2 both. Alternately, the air may be recirculated through the aerosol generator.

### 3 EXAMPLE

4 A filling device was set up according to the schematic of FIG. 6. The channel was  
5 fabricated of 1/4-inch thick polycarbonate sheet. The channel width was 40-mm and its  
6 height was 6-mm. A blister pack pocket, formed of 6-mil polyvinyl chloride, having a  
7 depth of 4-mm and a diameter of 6-mm was supported on a circular electrode 25 having  
8 a diameter of 4-mm.

9 The charge source, consisting of glass core rod 43, spiral wire electrode 47 and  
10 four glass coated wire 45 spaced at intervals around the periphery of the core rod, was  
11 obtained from Delphax Systems, Canton, MA. Delphax customers employ these rods in  
12 discharging (erasing) latent images on Delphax high-speed printer drums.

13 Spiral winding 47 was maintained at ground potential and glass coated tungsten  
14 wire 45 was excited using 2300 volt peak-to-peak ac at a frequency of 120 kHz. A Trek  
15 high voltage amplifier was employed to provide square wave switching of deposition  
16 electrode 25 at a frequency of 35 Hertz. The output voltage was switched between  
17 +5kV and -5kV. The duty cycle was set so that negative charges were extracted for 10%  
18 of the square wave period leaving positive charge extraction to occur over 90% of the  
19 duty cycle.

20 An aerosol consisting of lactose powder, having a particle size in the range of  
21 about 3 to about 7 microns, was suspended in a flowing stream of nitrogen gas. The

1 lactose was aerosolized by the turbulent action of pressurized nitrogen in a Wright Dust  
2 Feed aerosolizer manufactured by BGI Inc., Waltham, MA. The aerosol concentration  
3 was about 1 microgram/cm<sup>3</sup> and the channel flow velocity was adjusted to 30 cm/sec.

4 Charging and deposition potentials were applied for a period of two minutes  
5 during aerosol flow. A well-defined mass of powder, measured and found to be 1 mg,  
6 was formed at the bottom of the blister pack pocket. No powder deposition was found  
7 at the blister pack walls or on the bottom of the channel.

8 Subsequent experimental runs established that the mass deposited was  
9 proportional to the deposition time over the time intervals of ½ to 5 minutes.

10 With the present invention, it is also possible to multiplex the operation of two or  
11 more deposition zones served from a single aerosol source by configuring deposition  
12 zones along the aerosol path and selectively applying an alternating deposition field at  
13 one deposition zone at a time. Aerosol particles passing into a deposition zone where  
14 no alternating deposition field exists simply pass through the deposition zone  
15 whereupon they can pass into a next deposition zone.

16 Although various embodiments which incorporate the teachings of the present  
17 invention have been shown and described in detail herein, many other varied  
18 embodiments that still incorporate these teachings may be made without departing  
19 from the spirit and scope of the present invention. For example, the aerosol particles  
20 may comprise carrier particles which may comprise inert substrates including  
21 biocompatible metal particles coated with a bioactive agent.

CLAIMS

1. A method for depositing particles from an aerosol onto a dielectric substrate comprising the steps of charging said aerosol particles, positioning said charged aerosol particles in a deposition zone proximate to said dielectric substrate, and applying an alternating electric field in said deposition zone by which said charged particles are removed from the aerosol and deposited on said dielectric substrate thus forming a deposit.

2. The method according to claim 1, wherein said deposit has relatively more mass than a deposit that can be formed using a static electric field.

3. The method according to claim 1, wherein said aerosol particles are charged.

4. The method according to claim 1, wherein said aerosol particles comprise particles of dry powder.

5. The method according to claim 1, wherein said aerosol particles comprise liquid droplets.

6. The method according to claim 4, wherein said dry powder particles are triboelectrically charged.

7. The method according to claim 5 wherein said liquid droplets are charged by a charge injector during droplet formation.

8. The method according to claim 1, wherein said aerosol particles comprise a pharmaceutical.

1           9.     The method according to claim 4, wherein said dry powder particles  
2 comprise carrier particles coated with a bioactive agent.

3           10.    The method according to claim 3, wherein said aerosol particles have a  
4 higher charge to mass ratio than is achievable using triboelectric charging.

5           11.    The method according to claim 10, wherein said charged aerosol particles  
6 achieve a relatively higher velocity than that achievable with triboelectrically charged  
7 particles thereby forming said deposit more quickly.

8           12.    The method according to claim 1, wherein said aerosol particles are  
9 charged within said deposition zone.

10          13.    The method according to claim 1, wherein said aerosol particles are  
11 charged outside of said deposition zone.

12          14.    The method according to claim 1, wherein said alternating electric field  
13 has a magnitude between 1KV/cm and 30KV/cm.

14          15.    The method according to claim 1, wherein the frequency of said  
15 alternating electric field is between 1Hz and 100KHz.

16          16.    The method according to claim 1, wherein the duty cycle of said  
17 alternating field is substantially different than 50%.

18          17.    The method according to claim 16, wherein said duty cycle is 90%.

19          18.    The method according to claim 1, wherein said alternating electric field is  
20 formed between a first electrode positioned at an end of said deposition zone opposite

1 to and facing said dielectric substrate and a second electrode in contact with said  
2 dielectric substrate on the opposite side of where said deposit is formed.

3 19. The method according to claim 18, wherein said first electrode is an  
4 element of an ion emitter.

5 20. The method according to claim 19, wherein said aerosol particles are  
6 discharged after being deposited.

7 21. The method according to claim 18, wherein the contact area of said second  
8 electrode with said dielectric substrate determines the location of said deposition.

9 22. The method according to claim 1, wherein substantially all of said aerosol  
10 particles are removed from said aerosol to form said deposit.

11 23. The method according to claim 1, wherein the gas of said aerosol is  
12 predetermined.

13 25. The method according to claim 1, wherein said dielectric substrate  
14 comprises a packaging medium.

15 26. The method according to claim 25, wherein said packaging medium  
16 comprises a blister, tablet, capsule or tablet.

17 27. The method according to claim 26, wherein the blister comprises a plastic  
18 or metal foil blister package.

19 28. The method according to claim 1, wherein said dielectric substrate  
20 comprises a pharmaceutical carrier.

1           29.    The method according to claim 1, wherein said dielectric substrate  
2 comprises a carrier for carrying said deposit from said deposition zone to another  
3 location for further processing.

4           30.    The method according to claim 1, wherein said dielectric substrate is  
5 edible.

6           31.    The method according to claim 3, wherein said ion emitter comprises a  
7 corona wire or corona point.

8           32.    The method according to claim 3, wherein said ion emitter comprises a  
9 silent electric discharge device.

10          33.    The method according to claim 3, wherein said ion emitter comprises an  
11 ionizing radiation source.

12          34.    The method according to claim 12, wherein said aerosol particles are  
13 charged by an ion emitter.

14          35.    The method according to claim 22, wherein the mass of said deposit is  
15 controlled by integrating the mass of said aerosol particles over a period of time.

16          36.    The method according to claim 35, wherein said period of time is  
17 determined by the measured mass of said aerosol particles.

18          37.    The method according to claim 22, wherein multiple deposits may be  
19 made using multiple deposition zones supplied from a single aerosol source by  
20 multiplexing the application of the alternating deposition field between the deposition  
21 zones.



1           38.    A controlled quantity of powder carried on a substrate, comprising a  
2 plurality of layers of said powder in which adjacent layers carry opposite charges.

3           39.    A controlled quantity according to claim 38, wherein said powder  
4 comprises a pharmaceutical.

5           40.    A controlled quantity according to claim 38, wherein said substrate  
6 comprises a packaging medium.

7           41.    A controlled quantity according to claim 40, wherein said packaging  
8 medium comprises a blister, tablet, capsule or tublet.

9           42.    A controlled quantity according to claim 41, wherein said blister  
10 comprises a plastic or metal foil blister package.

11          43.    An apparatus for depositing onto a substrate controlled quantities of  
12 particulate material from a source of said material, said apparatus comprising a charge  
13 generator for applying a predetermined electrostatic charge to particles of said material  
14 upstream of a deposition zone in which said substrate is located, and a controller for  
15 repeatedly varying the polarity of charge being applied to said material and to said  
16 substrate.

17          44.    The apparatus according to claim 43, wherein the controller comprises a  
18 switch oscillator.

19          45.    The apparatus according to claim 43, wherein the controller includes a  
20 clock for varying the polarity of charge over time.

1           46.    The apparatus according to claim 43, wherein said controller is adapted to  
2 switch polarity applied to said powder and to said substrate in synchronization.

3           47.    The apparatus according to claim 43, and including sensors for measuring  
4 the mass flow of aerosol particles that pass into and out of the deposition zone.

5           48.    A method for depositing particles from an aerosol onto a substrate that  
6 comprises moving an aerosol through a deposition region, providing means for  
7 electrically charging said particles, and providing an alternating electric field between  
8 said substrate and said aerosol particles whereby said particles are deposited on the  
9 surface of said substrate.

10          49.    The method according to claim 48, wherein said particles are solid.

11          50.    The method according to claim 48, wherein said particles are liquid.

12          51.    The method according to claim 48, wherein said particles comprise carrier  
13 particles coated with a bioactive agent.

14          52.    The method according to claim 48, wherein said particles comprise a  
15 pharmaceutical.

16          53.    The method according to claim 48, wherein said aerosol carrier is nitrogen  
17 gas.

18          54.    The method according to claim 48, wherein said substrate comprises a  
19 blister pack.

20          55.    The method according to claim 48, wherein said substrate is comprised of  
21 an electrically insulating material.

1           56.    The method according to claim 48, wherein said substrate is comprised of  
2 an electrically conducting material.

3           57.    The method according to claim 48, wherein said electrically charging  
4 means employs a corona wire.

5           58.    The method according to claim 48, wherein said electrically charging  
6 means employs corona emitting points.

7           59.    The method according to claim 1, wherein said electrically charging  
8 means includes a charge source comprising a solid dielectric member, a first electrode  
9 substantially in contact with one side of said solid dielectric member, a second electrode  
10 substantially in contact with an opposite side of said solid dielectric member, with an  
11 edge surface of said second electrode disposed opposite said first electrode to define an  
12 air region at the junction of said edge surface and said solid dielectric member, and  
13 means for applying an alternating potential between said first and second electrodes of  
14 sufficient magnitude to induce ion producing electrical discharges in the air region  
15 between the dielectric member and the edge surface of said second electrode.

16           60.    The method according to claim 48, wherein said electrically charging  
17 means includes triboelectric charging of said aerosol particles.

18           61.    The method according to claim 48, wherein said electrically charging  
19 means includes induction charging of said aerosol particles.

20           62.    The method according to claim 48, wherein said aerosol particles are  
21 charged outside of said deposition region.

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63. The method according to claim 48, wherein said aerosol particles are charged within said deposition region.

64. The method according to claim 48, wherein said electrically alternating field has a magnitude between about 1 kV/cm and about 30 kV/cm.

65. The method according to claim 48, wherein said electrically alternating field has a frequency of oscillation between about 1 Hz and 100 kHz.

66. The method according to claim 48, wherein the duty cycle of the alternating field is adjusted to provide maximum efficiency of said particle deposition.

67. The method according to claim 48, wherein said electrically alternating field is formed between a first electrode positioned at one side of said deposition region opposite and facing said substrate and a second electrode contiguous to said substrate.

68. The method according to claim 48, wherein the pattern of deposited material is defined by the geometry of said alternating electric field.

69. The method according to claim 48, wherein the pattern of deposited material is defined by an electrically conducting mask disposed adjacent said charging means.

70. The method according to claim 48, wherein the aerosol particle mass flow is monitored whereby the mass of deposited particles is controlled.

71. The method according to claim 48, wherein multiple deposits may be made using multiple deposition regions supplied from a single aerosol source by

1 multiplexing the application of the alternating deposition field between the deposition  
2 regions.

3 72. A pharmaceutical unit dose medicament powder package wherein the  
4 powder is deposited using electrostatic means to form alternately charged layers of said  
5 powder.

6 73. The package of claim 72, wherein said electrostatic means includes  
7 moving an aerosol through a deposition region, providing means for electrically  
8 charging said medicament powder, and providing an alternating electric field between  
9 said powder package and said aerosol.

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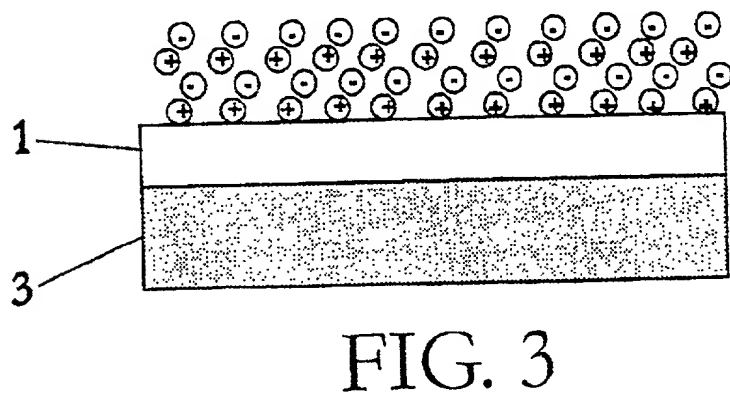
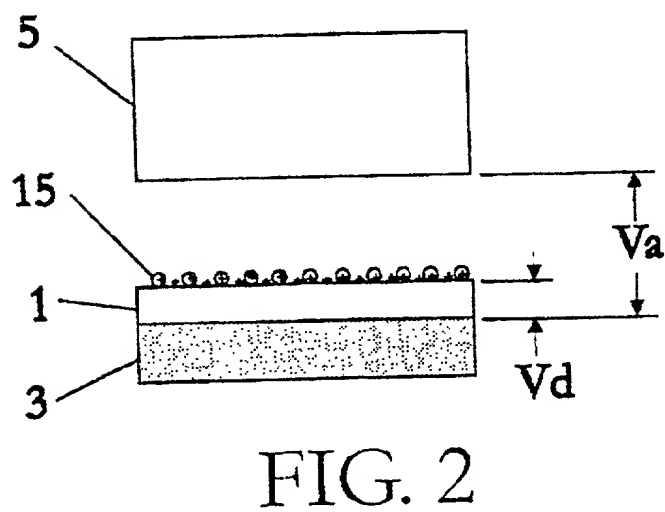
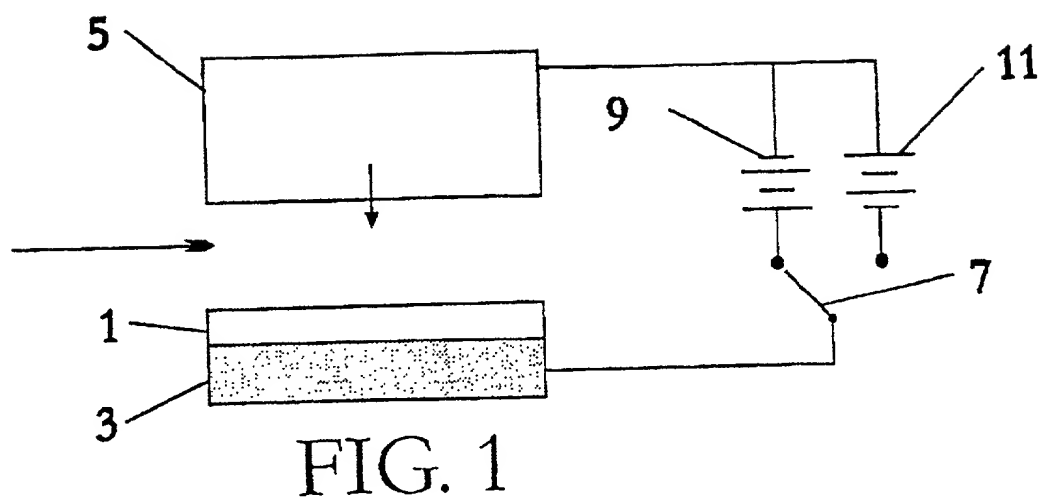
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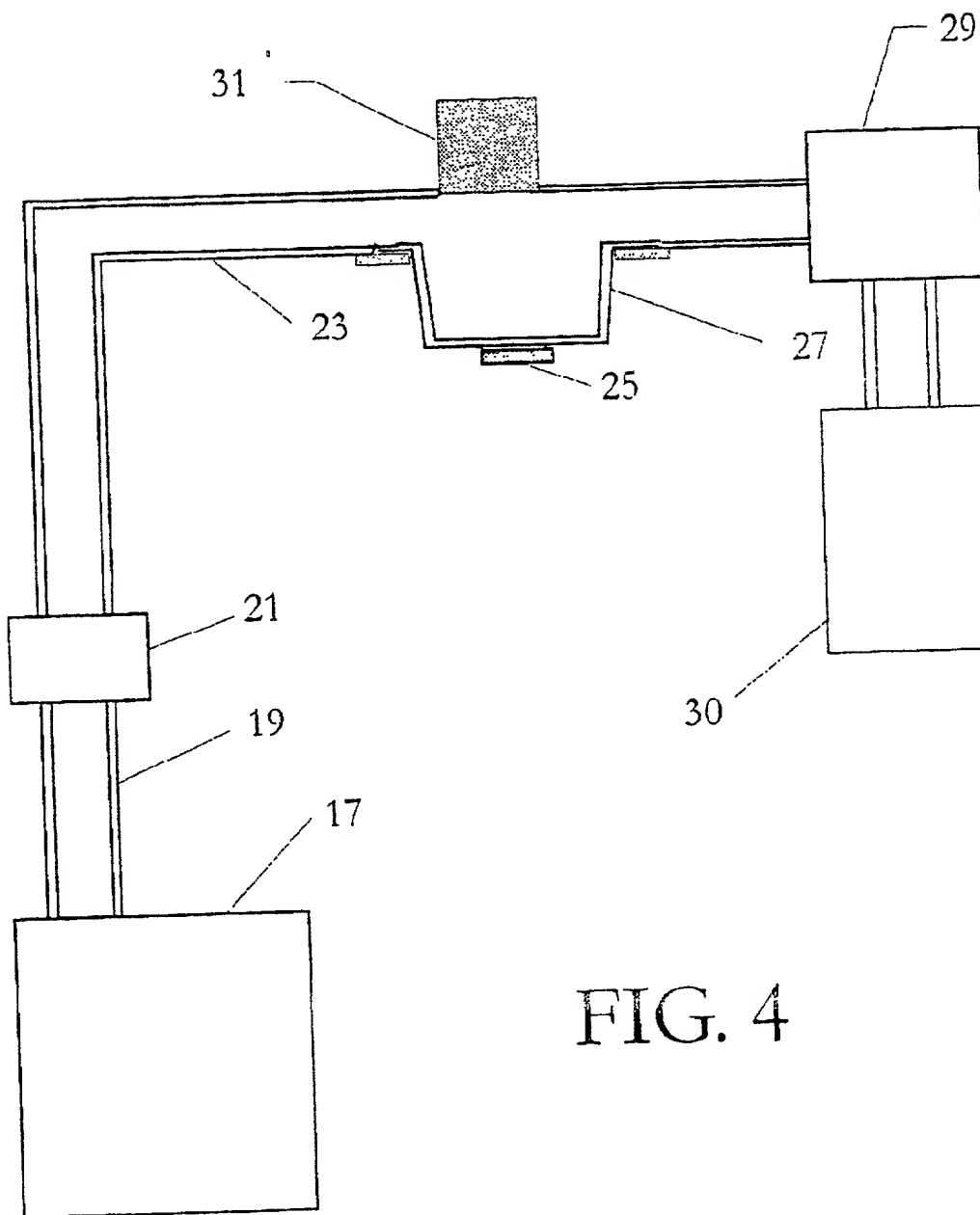


FIG. 4



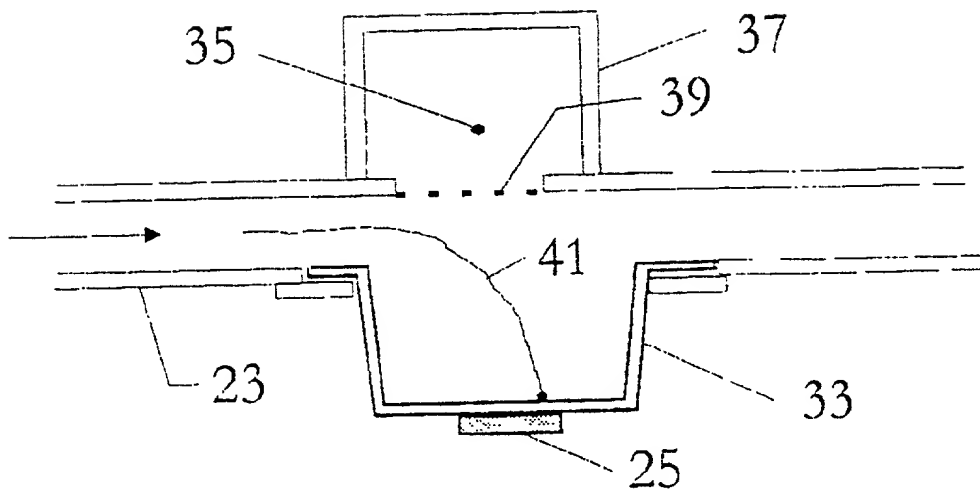


FIG. 5

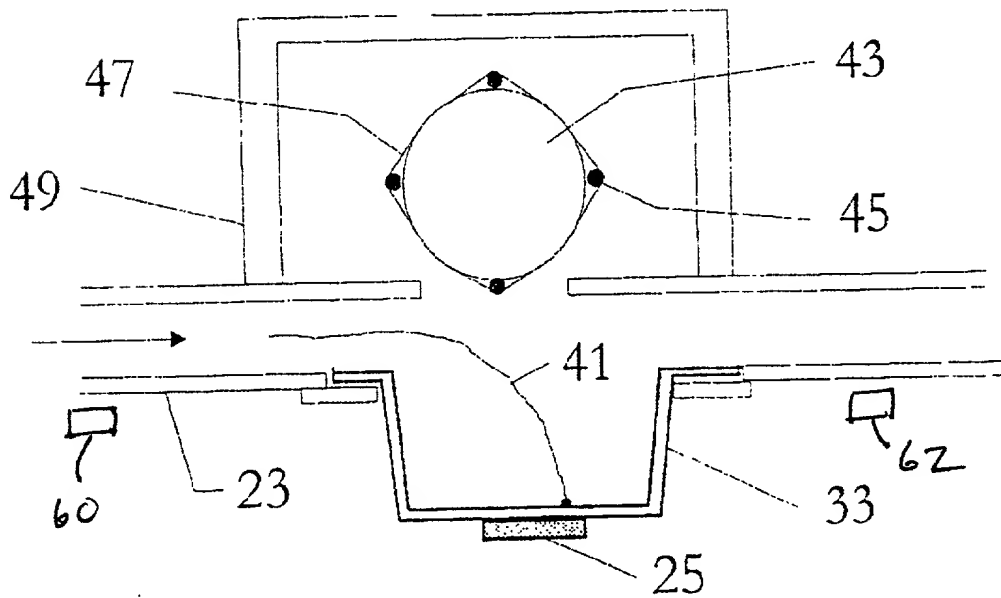


FIG. 6

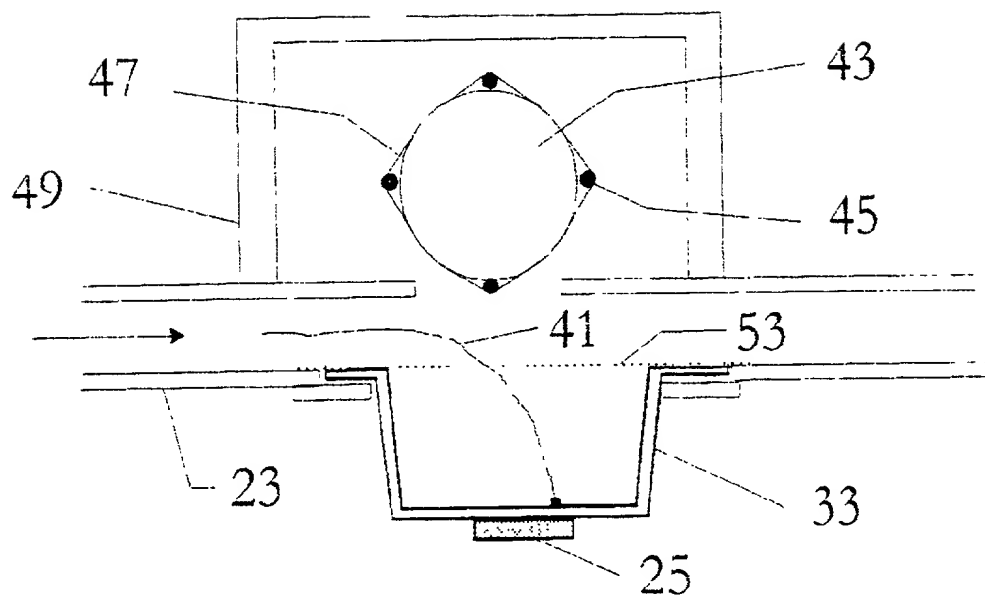


FIG. 7